29. (New) The method of claim 24, wherein said specimen further comprises one, or more than one, non-blood substitute interferent.

30. (New) The method of claim 29, wherein said one or more than one non-blood-substitute interferent is selected from the group consisting of intralipid (IL), bilirubin (BR), biliverdin (BV), turbidity and a mixture thereof.

REMARKS

Reconsideration and withdrawal of the rejections of the claims in view of the amendments and remarks presented herein is respectfully requested.

Claims 8 and 10-12 are amended; claims 1, 5-7, 9, and 13-22 are canceled; and claims 23-30 are added. As a result, claims 8, 10-12, and 23-30 are now pending in this application.

Support for the new and amended claims can be found throughout the specification. For instance, support for the phrase "A method of determining the concentration of an analyte in a specimen comprising a blood substitute interferent" can be found at page 4, lines 17-19 and 20-24; and page 5, lines 5-9. The phrase "or reflectance" in step (iii) of claim 8 is supported, e.g., at page 9, lines 16-17. The phrase "wherein the measuring is performed prior to or in the absence of any reaction step that generates a chromophore performed on said specimen" of claim 8 is supported at page 2, line 3-7. The phrases "measuring an initial concentration of said one or more than one analyte in said specimen" and determining "a corrected concentration of said one or more than one analyte" of claim 8 are supported, e.g., at page 4, lines 9-11 and page 5, lines 7-9. The phrase "linear equation" in claim 8 is supported, e.g., at page 4, line 20; page 5, lines 15 and 17-18; page 13, lines 3-7; page 18, lines 14-16; and page 20, line 17. The phrase in claim 8 "using a slope from said one or more than one linear equation from step (ii), said concentration from step (iv), and said initial concentration from step (v), to determine a corrected concentration of said one, or more than one analyte" is supported, e.g., at page 13, lines 3-6, 11-14, and 18-22; page 14, lines 8-13, page 18, line 18 to page 20, line 4; and page 23, lines 4-6. The amendments to claims 10-12 are to clarify and correct typographical errors. Support for amended claim 23 is

the same as support for claim 8. Claim 24 is supported by originally filed claims 4 and 16 of the International application no. PCT/CA97/00759. The phrase "measuring an absorbance of radiation of said specimen" of claim 24 is supported, e.g., at originally filed claim 4. The phrase "incorporating said absorbance measured in step (i) into a first calibration algorithm to determine the presence, concentration, or both, of said blood substitute interferent" of claim 24 is supported at originally filed claim 4. The phrase "wherein the measuring is performed prior to or in the absence of any reaction step that generates a chromophore performed on said specimen" of claim 24 is supported at page 2, lines 3-7. The phrase "incorporating said absorbance measured in step (i) into a second calibration algorithm to determine the presence, concentration, or both of Hb liberated from blood cells" of claim 24 is supported, e.g., at originally filed claim 1. The phrase "wherein a positive concentration value of blood substitute interferent, or Hb, is an indicator of pseudo-hemolysis, or hemolysis, respectively" of claim 24 is supported, e.g., at originally filed claim 16. Claim 25 is supported, e.g., at originally filed claims 8, 14, and 15. Claim 26 is supported, e.g., at originally filed claims 3 and 12; and at page 14, lines 19-22. Claim 27 is supported, e.g., at originally filed claim 14. Claim 28, is supported, e.g., at originally filed claim 14 and at page 14, lines 19-22. Claim 29 is supported, e.g., at originally filed claims 16 and 17. Claim 30 is supported, e.g., at originally filed claims 14 and 17; and at page 24, lines 3-6.

The 35 U.S.C. §112 Rejection of the Claims

Claims 1 and 7 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 1 and 7 have been canceled, obviating this rejection.

The 35 U.S.C. §103 Rejection of the Claims

Claims 1 and 5-22 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sagusa in view of Gimpel, Simon and Christenson, Leissing or Mullins.

The Examiner's rejection of claims 1, 5-7, 9, and 13-22 has been rendered moot by the cancellation of these claims. Insofar as this rejection is applied to the pending amended claims, it is respectfully traversed.

As the Examiner has noted, the Sagusa patent teaches a colorimetric method for measuring components in a sample in the presence of interfering chromogens. In the method disclosed in the Sagusa patent, a color former is added to blood samples for coloring, and measurements for specific components are determined based on the light absorbance caused by the coloring. However, no color-forming reaction is performed on the blood serum specimen prior to measuring an absorbance or reflectance of radiation of the specimen to predict the concentration of the blood substitute interferent in the sample in the methods claimed in the present application. To clarify this point, claim 8 has been amended to specify that no reaction step that generates a chromophore is performed on the specimen prior to measuring an absorbance or reflectance of radiation of the specimen to predict the concentration of the blood substitute interferent in the specimen. In addition, new claim 24, which is based on the subject matter of cancelled claim 17, also recites a measurement step that is conducted on a specimen, on which no color-forming reaction step is performed prior to the measurement step.

Christenson et al., disclose that haemoglobin-based blood substitutes interfere with routine chemical tests, and the dilution of the sample is suggested as a way to avoid interference. There is no teaching or suggestion in Christenson et al., as to how an interferent may be identified and/or quantified in a blood sample comprising a blood substitute. Rather, Applicant submits that Christenson helps define the problem in the art that the present invention is solving, that being determining the concentration of a blood substitute interferent in a sample or determining the concentration of an analyte in a sample containing an interfering blood substitute.

Leissing et al., disclose modifications of clinical chemistry methods to overcome interferences from diaspirin crosslinked hemoglobin (DCLHb). The abstract teaches that filtering samples through an Amicon Centrifree micropartition system can remove concentrations of DCLHb up to 5000 mg/dl, producing a filtrate with molecular weight constituents less than 30,000 daltons. Furthermore, for the detection of some analytes, dilution of the sample is

required, in a method similar to that disclosed in Christenson. Leissing et al. do not teach or suggest the subject matter that is disclosed by the claims of the instant application. Leissing, as noted for Christenson, defines the problem in the art that the present invention is solving.

Mullins et al., teaches that fluosol may lead to potential errors in the analysis of blood specimens. There is no disclosure or suggestion as to how an analyte may be identified and/or quantified in a blood sample that contains a blood substitute. Rather, Mullins et al. also helps to identify the problem that the present invention is addressed to solving.

Gimpel et al., discloses a method of measuring total bilirubin concentrations in cerebrospinal fluid based on diazotization of bilirubin. There is no teaching or suggestion for the determination of the concentration of an analyte in the presence of a blood substitute interferent.

Simon et al., teaches that iron dextran therapy may cause a red-brown discolouration of the plasma simulating a hemolytic transfusion reaction. The method used in Simon et al. to detect the iron, comprises adding Gomori's iron stain (page 342, last paragraph, left hand column) and obtaining a blue color. There is no suggestion or disclosure in Simon of a method that involves determining the concentration of a blood substitute interferent contained in a specimen. Nor is there a disclosure of using a method involving measuring the absorbance or reflectance of a specimen, wherein no reaction that generates a chromogen is performed on the specimen prior to measuring its absorbance or reflectance.

Sagusa, in combination with Gimpel, Simon, Christenson, Leissing and Mullins, do not disclose or suggest all the elements of any of the pending claims. None of them teach or suggest a method for determining the concentration of an analyte in a specimen containing a blood substitute interferent that involves predicting the concentration of the blood substitute interferent, as is recited in claims 8, 10-12, 23, and 24-28. None disclose or suggest a method of determining the concentration of an analyte in a specimen that involves measuring an initial concentration of the analyte and then using a predicted concentration of a blood substitute interferent to determine a corrected concentration of the analyte, where the method involves measuring an absorbance or reflectance of radiation of the specimen, wherein the measuring step is performed prior to or in the absence of any reaction step that generates a chromophore performed on the specimen, as is recited in claims 8, 10-12, 23, and 25-28. Thus, alone or combined, the references do not teach

or suggest all the elements of any of the present claims. Furthermore, the references provide no suggestion or motivation to modify reference teachings to arrive at the invention of claims 8, 10-12, 23, and 25-28. The cited references also provide no expectation of success at practicing a method of determining the concentration of an analyte in a specimen containing a blood substitute interferent, where the method involves measuring an absorbance or reflectance of radiation of the specimen, wherein the measuring step is performed prior to or in the absence of any reaction step that generates a chromophore performed on the specimen. Thus, the cited references provide none of the three requirements for a prima facie case of obviousness over claims 8, 10-12, 23, and 25-28.

Likewise, none of the cited references discloses or suggests a method of determining the presence of true hemolysis, pseudo hemolysis caused by a blood substitute interferent, or both, in a specimen that involves measuring an absorbance of radiation of the specimen, wherein the measuring is performed prior to or in the absence of any reaction step that generates a chromophore performed on the specimen, as is recited in claims 24 and 29-30. None of them disclose or suggest measuring the absorbance of radiation of the specimen, wherein the measuring is performed prior to or in the absence of any reaction step that generates a chromophore performed on the specimen, and using the absorbance to determine the presence, concentration, or both, of a blood-substitute interferent, as is recited in claims 24 and 29-30. Thus, the references, alone or combined, do not teach or suggest all the elements of claims 24 and 29-30. Furthermore, the references provide no suggestion or motivation to modify reference teachings to arrive at the invention of claims 24 and 29-30.

The cited references also provide no expectation of success at practicing a method for determining the presence of true hemolysis, pseudo hemolysis caused by a blood substitute interferent, or both, in a specimen, comprising the steps of (i) measuring an absorbance of radiation of the specimen, wherein the measuring is performed prior to or in the absence of any reaction step that generates a chromophore performed on the specimen; (ii) incorporating the absorbance measured in step (i) into a first calibration algorithm to determine the presence, concentration, or both, of the blood substitute interferent; and (iii) incorporating the absorbance measured in step (i) into a second calibration algorithm to determine the presence concentration,

or both of Hb liberated from blood cells; wherein a positive concentration value of blood substitute interferent, or Hb, is an indicator of pseudo-hemolysis, or hemolysis, respectively.

Thus, the cited references do not satisfy any of the three requirements for a prima facie case of obviousness over claims 24 and 29-30.

Accordingly, withdrawal of the rejections of the claims under 35 U.S.C. § 103(a) over Sagusa in view of Gimpel, Simon and Christenson, Leissing or Mullins is respectfully requested.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612 349-9580) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Box AF, Commissioner of Patents, Washington, D.C. 20231, on this 15th day of October, 2002.

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